VOLUME-7, ISSUE-7, JULY-2018 • PRINT ISSN No 2277 - 8160

Original Research Paper

Anesthesiology

HIGH-VOLUME LOW-CONCENTRATION INTRAPERITONEAL BUPIVACAINE FOR POST-LAPAROSCOPIC CHOLECYSTECTOMY ANALGESIA : A PROSPECTIVE RANDOMISED CONTROLLED STUDY.

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ABSTRACT Pain is considerable after laparoscopic cholecystectomy. This study was conducted to evaluate results of high-volume low concentration bupivacaine for post-operative analgesia in Laparoscopic Cholecystectomy. Sixty patients undergoing LC were included in this study. Patients were divided into two ($n = 30$) groups. In Group S intraperitoneal irrigation was done with 300 ml of normal saline. In Group B 25 ml of 0.5% (125 mg) bupivacaine was added to 275 ml of normal saline for intraperitoneal irrigation during and after surgery. Post-operative pain assessment,duration of analgesia (DOA), total rescue analgesic requirement, nausea and vomiting were recorded for the initial 24 h post-operatively. In Group B mean DOA was more and cumulative requirement of rescue analgesic was less than that in Group B. There was no significant difference in incidence of nausea and vomiting between the groups. High-volume low-concentration of intraperitoneal bupivacaine significantly increases post-operative DOA and reduces opioid requirement after LC.

KEYWORDS : Analgesia, bupivacaine, laparoscopic cholecystectomy

INTRODUCTION

Laparoscopic cholecystectomy is considered the gold standard treatment for benign gallbladder disease. It has improved surgical outcome in terms of reduced pain and convalescence compared to conventional cholecystectomy.[1,2] However, the postoperative pain is considerable. Because postoperative pain after laparoscopic surgery is complex, specialists suggest that effective analgesic treatment should be a multimodal support. It includes blocking the sensitive afferents (infiltrating the skin with a local anesthetic before any incision), administration of an opioid perioperatively, irrigating a local anesthetic in the peritoneal cavity, providing the patient with fluids and electrolytes.[3,4,5,6]. Recently, intraperitoneal instillation of different local anaesthetics (LAs) has been gaining popularity for post-operative analgesia in LC. Most of the studies have used bupivacaine irrigation of peritoneal cavity in low volume (20 ml to 100 ml) and high concentration (0.5%–0.125%). However, their analgesic action is effective for only a few hours in the post-operative period.[7,8]

This study was conducted to evaluate the results of high-volume (300 ml) low-concentration (0.04%) bupivacaine for post-operative analgesia in Laparoscopic Cholecystectomy.

METHOD

This prospective, randomised, double-blind study was approved by the Hospital Ethics Committee. ASA grade I and II patients of either sex, between 20 and 60 years of age, undergoing elective Laparoscopic Cholecystectomy under general anaesthesia, were enrolled for the study. Written informed consent was obtained after due counselling. Patients were familiarised with numeric pain rating scale (NPRS), where 0 represented no pain and10 represented maximum possible pain. Exclusion criteria included pregnancy, allergy to LAs, acute pancreatitis, choledocholithiasis, chronic pain, current opioid use, inability to comprehend NPRS and conversion of Laparoscopic Cholecystectomy to open cholecystectomy. All the patients fasted for 8 h before surgery and were given uniform premedication with intravenous (IV) injection midazolam 0.025 mg/kg, fentanyl 2 μg/kg and ondansetron 0.1 mg/kg. General anaesthesia was induced with IV 2 mg/kg of propofol, muscle relaxation was obtained with IV 0.1 mg/kg of vecuronium bromide and trachea was intubated. Anaesthesia was maintained with 0.8%–1% isoflurane in a mixture of oxygen and nitrous oxide. Intra-abdominal pressure was restricted to ≤12 cm H2O during surgery. All patients also received IV 1.5 mg/kg of diclofenac sodium for analgesia during surgery. No further analgesic was given during surgery. Randomisation was done by chit in box method and patients were divided into two groups of 30 patients each, i.e., Group S and Group B. Random group assigned was enclosed in a sealed envelope to ensure concealment of allocation sequence. After transferring the patient to the operation theatre, sealed envelope was opened by the anaesthesiologist, not involved in the study, who then prepared the drug solution according to randomisation. The study was double blinded.In Group S, 300 ml of normal saline was used as the irrigation fluid. In Group B, 25 ml 0.5% (125 mg) bupivacaine was added to 275 ml of normal saline for intraperitoneal irrigation.The surgeon used this irrigation fluid during dissection of gall bladder and aspirated the fluid after complete dissection. After gall bladder extraction, the surgeon was asked to irrigate the surgical bed as well as the peritoneal cavity with rest of the irrigating fluid. Patient was placed in Trendelenburg's position with right lateral tilt to facilitate dispersion of drug solution in the sub-hepatic region for 5 min. It was done through subcostal trocar under direct laparoscopic control. Irrigating fluid was then aspirated, drain was placed and surgical ports were closed. Isoflurane and nitrous oxide were stopped. Reversal of residual neuromuscular blockade was done with a mixture of neostigmine (0.04 mg/kg) and glycopyrrolate (0.01 mg/kg) and the patient was extubated. Patients were subsequently transferred to the recovery area. The post-operative nursing staff, unaware of the patient's group, recorded NPRS at fixed intervals, i.e., immediately after extubation, at 30 min, 1, 2, 4, 6, 8, 12 and 24 h post-operatively and whenever the patient complained of pain. IV injection tramadol 2 mg/kg was given as rescue analgesic whenever the patient experienced pain equal to or more than 4 in the NPRS. The length of time between extubation and the first request for rescue analgesic was recorded, which was called as duration of analgesia (DOA).The primary aim of the study was to compare DOA between two groups at different time intervals. Secondary objective was to record the NPRS score,cumulative requirement of rescue analgesic used in 24 h post-operative period, nausea and vomiting.

Data analysis was performed using SPSS version 16.0 for Windows. Data were presented as mean ± standard deviation or number of patients. Demographic data, duration of surgery, NPRS scores at different time intervals, DOA and cumulative requirement of rescue analgesic were compared between the groups by analysis of variance and Tukey honest significant difference was used for *post hoc* multiple comparisons. Pearson Chi-square test was applied to analyse differences in categorical values. The value of $P < 0.05$ was considered statistically significant.

RESULTS

Sixty patients were randomly divided into two groups of 30 patients each. After recruitment, none of the patients were excluded from the study due to conversion from Laparoscopic Cholecystectomy to open cholecystectomy. Demographic profile in terms of age, weight and sex distribution, as well as duration of surgery, was comparable

in both the groups [Table 1]. All the patients in both the groups received similar intra-operative analgesics (fentanyl 2 µg/kg and diclofenac sodium 1.5 mg/kg). DOA in Group S were 0.06 ± 0.172 h (3.6 ± 10.32 min) and that in Group B was 16.55 ± 8.64 h (P = 0.00).

Cumulative requirement of tramadol in 24 h in Group S was 123.33 ± 43.01 mg which was significantly higher(P = 0.00) than Group B (25.63 ± 43.01 mg) [Table 2]. At extubation, patients of Group S reported significantly higher NPRS score as compared to Group B (P = 0.0) [Table 2]. In Group S, out of 30 patients, 28 required rescue analgesic immediately after extubation, and the rest two patients required rescue analgesic within half an hour post-operatively.

Three patients required one additional dosage of rescue analgesic over 24 h. In Group B, only two patients required rescue analgesic within half an hour post-operatively. Overall, only nine patients out of 30 required rescue analgesic in 24 h and none required any additional dosage. Nausea and vomiting occurred in 4 patients in each group. There were no complications of bupivacaine in the study group.

Table 1.Demographic and operative characteristics of the patients

Variable	Mean±SD		*P*
	Group S	Group B	
Age (years)	41.97±12.0	37.03±10.52	0.303
Sex			
Male	7	4	
Female	23	26	
Weight (kg)	53.87±8.32	54.57±7.27	0.798
Duration of surgery (min)	57.90±8.47	58.77±8.97	0.878

SD – Standard deviation

Table 2.Duration of analgesia, requirement of tramadol and numeric pain rating score at various time intervals of patients.

Parameters	Group S	Group B	*P*
Duration of analgesia (h)	0.06±0.172	16.55±8.64	0.000
Cumulative requirement of tramadol in 24 h (mg)	123.33±43.01	25.63±43.01	0.000*
NRS at extubation	4.67±1.2	0.47±0.77	0.000*
30 min	1.44±1.88	0.80±1.06	0.148
1 h	0.83±0.88	1.17±0.95	0.301
2 h	1.17±0.74	1.53±0.97	0.189
4 h	1.47±0.50	1.70±0.95	0.504
6 h	1.70±0.59	2.23±1.27	0.663
8 h	1.57±0.62	1.37±0.61	0.599
12 h	1.47±0.73	1.77±0.67	0.234
24 h	1.27±0.45	1.17±0.46	0.631

*Significant P<0.05. NRS – Numeric pain rating scale

DISCUSSION

In this study, intraperitoneal instillation of high-volume low-concentration bupivacaine significantly increased DOA and reduced opioid requirement after LC. Early pain after LC is multifactorial.[5] It is derived from multiple situations: incision pain (somatic), deep intraabdominal pain (visceral), and shoulder pain (visceral pain due to phrenic nerve irritation).[4]This complex pain can be managed with multimodal and opioid sparing regimen to accelerate postoperative recovery.[9,10] In this study, both the groups received preoperative fentanyl and diclofenac sodium during surgery. In addition, irrigation of peritoneal cavity was done with bupivacaine,during as well as at the end of surgery in patients of Group B. Diclofenac sodium treated parietal pain, while bupivacaine provided visceral analgesia postoperatively. Bupivacaine was selected for irrigating peritoneal cavity as it is an amide type of LA that provides prolonged analgesia. Previous studies had used low volume (20 ml to 100 ml) high concentration (0.5% to 0.125%) instillation of bupivacaine in gall bladder bed and has been reported to be ineffective[11]to short-acting analgesia only.[8,9]This could be because a low volume of LA was not sufficient to cover the entire gall bladder bed nor address all factors causing visceral pain. High-volume low-concentration bupivacaine (300 ml, 0.04%) used in this study has not been previously reported. High volume used in this study was able to effectively cover a larger surface area of sub-hepatic space and the surrounding peritoneum, while its continuous use in irrigating fluid during surgery increased the contact period producing longer DOA. Supporting rationale for choice of high-volume low-concentration bupivacaine solution was a study by Gupta and Hopkins.[12] who reported that ED50 of bupivacaine is not dependent upon its concentration. While, Nunez *et al*.[13]reported more efficacious sensory block with high-volume low-concentration as compared to low volume high concentration of levobupivacaine in brachial plexus block.Overall requirement of tramadol on the day of surgery was 100% in Group S and 23% for Group B. Boddy *et al*[14]and Gupta in a systemic review reported no reduction in analgesic requirement with intraperitoneal instillation of bupivacaine. In both the systemic reviews, the volume of LAs used in different studies varied from 10 ml to 100 ml with concentrations ranging from 0.1% to 0.5%. Since in our study high-volume low-concentration (300 ml, 0.04%) bupivacaine gave long post-operative analgesia, the requirement of tramadol was significantly less in Group B. No significant difference was found in the incidence of nausea and vomiting between the groups. This may be attributed to the use of ondansetron in all the patients.[15] Previous studies have also demonstrated that bupivacaine instillation did not decrease the incidence of nausea and vomiting.[16]

CONCLUSION

Intraperitoneal irrigation with high-volume low-concentration bupivacaine significantly increases DOA and reduces opioid requirement after LC.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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